EXHIBIT 5

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In reaching the opinions set forth in this report, I am relying upon my background, training, and experience; the literature cited below; and generally available medical knowledge about asbestos-related diseases. I include by reference the opinions I have expressed in my expert reports and testimony in the WR Grace bankruptcy proceedings and in my report in this matter from December 2008.

I reviewed the expert reports submitted by Dr. Whitehouse and Dr. Frank in December 2008, and the attachments to that report. This report is a rebuttal to those reports. In his report Dr. Whitehouse (1) presents an analysis of mortality among his patients, (2) presents the basis for his opinion that asbestos exposure from Libby has resulted in rapid progression of pulmonary function loss, and (3) that the asbestos found in Libby vermiculite is more toxic than other asbestos used by other workers in the United States. Dr. Whitehouse relies in large part on his mortality study and the progression study from his 2004 paper for his opinions that pleural disease caused by exposure to the tremolite, winchite and richterite asbestos found as contaminants in the vermiculite ore mined in Libby Montana is much more likely to lead to severe lung function decline and death in patients than pleural disease caused by exposure to other types of asbestos. Here I will address each of those points in some detail, and explain why they do not support Dr Whitehouse's conclusions.

CARD Mortality Study

Dr. Whitehouse describes an analysis of deaths among the patients seen in the CARD clinic. As described in his report a total of 227 patients were identified as deceased through July 9, 2008. He reported that 41 were excluded because they had no diagnosis of asbestos related disease, no death certificate, no chart or chest film, or had no exposure before 1990. These cases were excluded to create a cohort exclusively of patients with asbestos-related disease. He then obtained death certificates and stated that he assigned cause of death according to the methods used by Dr. Selikoff in the 1992 papers referenced in the report. Based on this analysis of deaths among his patients, all of whom had a diagnosis of a non-malignant asbestos-related disease prior to death, he concludes that the death rate from asbestos-related disease in Libby is higher than that seen in the insulators' cohort, studied by Dr. Selikoff. He also concludes that "exposure to Libby asbestos is considerably more toxic to humans than was the predominately chrysotile exposure of the insulation workers."

I want to discuss several important aspects of the methods used by Dr. Whitehouse in his study of mortality that render these conclusions inaccurate.

1. His method for assembling the cohort for study
2. His method for determining cause of death
    a. for attributing a death to asbestos exposure
    b. his use of Dr. Selikoff's best evidence approach

(1) Dr. Whitehouse's method for assembling the cohort for study

Dr. Whitehouse studied cause of death in a case series of patients, not a population based cohort. A population-based cohort is defined, for example, as a group of individuals who all worked in the same facility, or who lived in a community; the cohort is intended to represent the entire population at risk. Dr. Whitehouse's study population is only a subset of the cohort of people who lived and worked in Libby Montana, a subset with symptoms and nonmalignant asbestos-related disease. Since his group of patients does not represent the entire group of Libby residents this analysis cannot be used to draw conclusions about asbestos-related mortality in the entire cohort of Libby.

The insulator cohort studied by Dr. Selikoff was a population based cohort; Dr. Selikoff enrolled the entire membership of insulation workers union as of 1/1/1967 in a prospective study. He included individuals whether or not they had a clinical diagnosis of non-malignant asbestos-related disease. The method used by Dr. Whitehouse to assemble a group of individuals for study is not comparable to the method used by Dr. Selikoff. A group of patients is clearly more likely to include individuals who are ill and sought care because of symptoms or disease.

To illustrate the difference between a case series and a cohort, let's look at a study of individuals who smoke cigarettes versus individuals who have COPD from cigarette smoking. The group with a diagnosis of COPD can be considered a case series if they are identified from a physician's practice or an emergency room. One study looked at the 1 year mortality rate of individuals with COPD who were admitted to an ICU with an exacerbation of COPD, and reported that 59% had died one year later [1]. Clearly, 60% of smokers do not die every year, so the presence of disease is a stronger predictor of death than simply the hazardous exposure. The presence of clinical symptoms, even without a diagnosis of COPD is also predictive of excess mortality. In a longitudinal study in France, mortality was closely related to dyspnea level ($p < 0.0001$) both in men and women, especially for grade 3 and over, even after adjusting on age, sex, smoking history and former occupation.[2] For heart disease, the risk of death is known to increase in the presence of known coronary artery disease, and similar examples abound. One simply cannot compare a case series of patients to a population-based cohort.

[1] Seneff MG, Wagner DP, Wagner RP, Zimmerman JE, Knaus WA. JAMA. 1995 Dec 20;274(23):1852-7. Hospital and 1-year survival of patients admitted to intensive care units with acute exacerbation of chronic obstructive pulmonary disease.

[2] Eur J Epidemiol. 2001;17(3):223-9. Dyspnea and 8-year mortality among elderly men and women: the PAQUID cohort study. Tessier JF, Nejjari C, Letenneur L, Filleul L, Marty ML, Barberger Gateau P, Dartigues JF.

(2) Dr. Whitehouse's method for determining cause of death, including his use of Dr. Selikoff's best evidence approach

a. Assigning cause of death

The standard death certificate is used in all U.S. states. The medical portion of the death certificate includes date and time of death and death pronouncement; a question about referral to the coroner; the cause of death section; a section about injuries; and the certifier's section, with signature.

Part I of the cause of death section allows for a description of the sequence of events leading to death, with the most immediate cause of death on line "a" and the underlying causes on lines "b," "c," and "d." Standard mortality analyses use the underlying cause of death as determined by a nosologist, someone specifically trained in determining cause of death. This is the process followed by the National Death Index in assigning cause of death.

Part II of the cause of death section is the place to report all other significant diseases, injuries, or conditions that contributed to the patient's death but that did not result in the underlying cause of death listed in part I. This section also might include another, less significant, sequence of causes related to the death, including, for example, the decedent's use of tobacco. The conditions listed in Part II of the death certificate are not generally used to determine cause of death.

Dr Whitehouse considered a death to be asbestos-related if there was any mention of asbestos disease, either as underlying cause or a significant cause, either in Part I or Part II of the death certificate. An individual whose primary cause of death was stroke but who also had asbestosis listed in part II of the death certificate would be classified by Dr. Whitehouse as an asbestos-related death. Dr. Selikoff's mortality study used the primary diagnosis as the cause of death for his study, and so Dr. Whitehouse's analysis is not comparable to Dr. Selikoff's (or Dr. Markowitz's) studies.

(b) Use of best evidence

Dr. Whitehouse compares the results of his mortality analysis to the results from Dr. Selikoff's insulators' studies, and states that he use the same method used by Dr. Selikoff to assign cause of death, using "best evidence".

Dr. Selikoff enrolled the entire membership of insulation workers union as of 1/1/1967 in a prospective study. On that date there were 17,800 men on the rolls of the International Association of Heat and Frost Insulators and Asbestos Workers in the United States and Canada. Starting in 1967 Dr. Selikoff and his colleagues maintained observation of the entire cohort with the assistance of the officials of the local unions. Whenever a member died Dr. Selikoff's team was notified, often both by the local union and by the health and welfare unit of the International office in Washington. In addition periodically the researchers sent lists of local union members assumed to be alive to each local union and requested confirmation of current vital status. Upon notification of death the researchers obtained the death certificate from the local union or from the appropriate state Department of Health. Local union officials were asked to complete a

specific mortality form that included information on the facility in which the death occurred, treating physicians, next of kin, and other pertinent data. The research team then requested from all treating facilities and all treating physicians clinical data and loan of available chest x-rays. All pathology facilities known or likely to have surgical or autopsy material were contacted and permission asked to borrow pathologic material. The clinical and pathological materials were reviewed by the research team, and cause of death ascertained according to the *best evidence* available.

When Dr. Selikoff reported the results in 1992 he found that there were discrepancies between cause of death on death certificate and cause of death using the best evidence method. When Dr. Selikoff described the discrepancies between the cause of death reported on death certificate and the cause of death according to the best evidence, he was comparing only *for the principal cause of death*. He described that this discordance was greatest for mesothelioma. He noted that the *fact* of mesothelioma was frequently present on the death certificate but this disease was not listed as the primary cause of death. Prior to 1999 the international classification of diseases (ICD) did not include a specific code for mesothelioma. With the 10th revision of the ICD, a specific code was assigned for mesothelioma; research had shown that the reporting of mesothelioma on death certificates has greatly increased with the ICD-10 revision [3]. Dr. Selikoff reported that the great majority of lung cancers were correctly identified as the primary cause of death on death certificate.

Dr. Whitehouse describes that he assigned cause of death according to the methods used by Dr. Selikoff, but does not provide additional detail. If he had followed Dr. Selikoff's methods he would have requested medical records from treating hospitals and other treating physicians, and autopsy material if available. In my review of the medical records available as exhibits in this matter, I did not see medical records from the time of death for individuals who died in the hospital. The records available for my review were medical records from Dr. Whitehouse and Dr. Black, and in some files records from other facilities. I saw no correspondence with medical facilities asking for records after a patient died. Below I provide details of several cases to that illustrate that Dr. Whitehouse did not follow the methods used by Dr. Selikoff.

> LB, L550-020, died in September 1999 at age 78 in the Kootenaii dialysis center. His death certificate lists the immediate cause of death as renal failure, with diabetes as the underlying cause. Other significant but not underlying conditions listed were prostate cancer, ASCAD, and ulcerative colitis. The file available for my review contained 12 pages, all of which were from the medical chart from Drs. Klock and Whitehouse from 1988. There were no records from the year immediately preceding this individual's death and none that related to his renal failure or the other conditions listed on his certificate. He is listed in Dr. Whitehouse's mortality study as having died from asbestos related disease based on a best evidence review. In my opinion this would not conform to the methods used by Dr. Selikoff.

[3] Int J Occup Environ Health. 2004 Jul-Sep;10(3):251-5. Malignant mesothelioma surveillance: a comparison of ICD 10 mortality data with SEER incidence data in nine areas of the United States. Pinheiro GA, Antao VC, Bang KM, Attfield MD.

WC, L550-086, died age 69 in Spokane Valley Hospital on 10/10/01 of chronic lymphocytic leukemia. The last notes in Dr. Whitehouse's records were from June 2001. There were no records in the file from Spokane Valley Hospital. In December 2000 Dr. Whitehouse wrote "…his current problems are obviously not asbestos-related but may well be that related to his leukemia, superimposed chronic respiratory infections along with GI bleeding." In a letter dated November 20, 2001 Dr. Whitehouse stated "Although he ultimately died of complications of leukemia his death was considerably hastened by the fact he had significant respiratory disease and was relatively intolerant of the anemia that occurred with his leukemia." His primary cause of death was clearly chronic lymphocytic leukemia.

SB, L550-074 died at home at age 64 on 2/7/07; her death certificate listed cause of death as ASCVD, with no mention of asbestosis. Dr. Whitehouse had assigned her a diagnosis of pleural thickening related to asbestos. That last note in a file from Dr. Whitehouse was July 11, 2005. Dr. Whitehouse did note that SB had had seven angioplasties, had several non-operable vessels everywhere and might need an amputation in her left leg for vascular disease. There was no evidence in this file that Dr. Whitehouse requested all her medical records from the treating physicians.

Based on my review of these cases and others, I conclude that Dr. Whitehouse did not follow the methods described by Dr. Selikoff in his 1992 paper for the use of best evidence.

It appears that if an individual had a clinical diagnosis of "asbestosis" or asbestos-related pleural disease then Dr. Whitehouse considered his or her death an asbestos-related death, even when the primary cause of death was dementia, stroke, coronary artery disease, congestive heart failure, cardiomyopathy, renal failure, gastrointestinal bleeding, sepsis, peritonitis, or another chronic disease that did not involve the lung. This method of assigning cause of death increases the number of asbestos-related deaths above what would be considered as asbestos-related if only the primary cause of death were used. Dr. Whitehouse's' methodology therefore makes it impossible to compare the asbestos related mortality in his patients to published studies of other cohorts, for other mortality studies of asbestos-exposed populations are based on the primary cause of death. Dr. Selikoff used his review of the best evidence to *reassign* the primary cause of death. Dr. Whitehouse does not appear to be re-assigning the primary cause of death, but rather assigning asbestos-related disease as a contributing cause of death if an asbestos-related diagnosis had been made.

Dr. Whitehouse's report draws a number of conclusions about deaths from asbestos-related disease in the Libby population, and how those patterns differ from patterns seen in other asbestos-exposed groups (see items 32 and 34, 41, 42). These comparisons are not valid. It may be the case that 46% of the CARD case series died with minimal or no interstitial disease (see p 24), but one cannot conclude that the asbestos-related pleural disease diagnosed by Dr. Whitehouse in his practice was the *primary or underlying cause* of death. As described above the methods Dr. Whitehouse used for assigning cause of death are not what are generally accepted in use for cohort mortality studies.

B. Dr. Whitehouse's opinion that eight of his patients died of pleural disease

I reviewed records for these eight individuals**.**

Three (AW, DR, JD) had extensive diffuse pleural thickening, and also had parenchymal asbestosis. These three individuals had occupational exposure at W.R. Grace, one for 2 1/2 years in the dry mill, one for 12 years at Zonolite with some in the dry mill, and the third in the rail yards for 27 years. In addition, one had congestive heart failure and another had significant obstructive lung disease.

A fourth case had pleural plaques in association with very significant obstructive lung disease (EO). This individual presumably had household exposure through her husband, who works for W.R. Grace. The fifth case (DA) had bilateral calcified pleural plaque and possibly mild fibrosis, but died of complications of his chronic lymphocytic leukemia. In my opinion the sixth case (FS) most likely had sleep apnea and no asbestos-related disease. The seventh case (CH) had a left pleural effusion and multiple pleural plaques found on thoracotomy. There are insufficient records for me to determine what other medical conditions she had, although in the months before her death she had a massive gastrointestinal bleed and then onset of severe congestive heart failure. Her file did not contain any pulmonary function testing. (Cannot find records for the eighth individual, FC).

After reviewing records on these individuals I would agree that the extensive diffuse pleural thickening in three of the cases could have been a contributing cause to their death. This diffuse pleural thickening occurred in three individuals with significant occupational exposure to asbestos. It is my opinion that the impairment from pleural disease in these three individuals is similar to what has been previously reported in other asbestos exposed populations, that diffuse pleural thickening involving blunting of the costophrenic angle can result in significant impairment of lung function. In my opinion pleural disease did not contribute to the death of the other five cases.

Rapid Loss of Lung Function in Patients with Pleural Disease

In his paper entitled *Asbestos-Related Pleural Disease Due To Tremolite Associated with Progressive Loss of Lung Function*, Dr. Whitehouse concludes that there is a progressive loss of pulmonary function in his patients exposed to tremolite asbestos. He states that prior research on this population has documented the presence of interstitial and pleural disease, but none document the rapid progression of loss of pulmonary function in such a large group of patients with predominantly pleural disease. He concludes that the number of patients with progressive loss of lung function is much higher than has been previously reported in studies with either chrysotile or amphibole asbestos exposure. He says it is apparent from these data that the majority of the 1500 persons who have radiologic changes of asbestos exposure are at increased risk for progressive loss of lung function from pleural changes alone, or from potential future development of interstitial fibrosis.

It is my opinion that limitations in the study design limit validity of the primary conclusion that this group of patients has rapid progressive loss of pulmonary function. In addition it is my opinion that one cannot extrapolate from this group of 123 patients to the larger cohort of 1500 people in Libby Montana with radiologic changes due to asbestos exposure.

(1) The first reason that Dr. Whitehouse's progression study of the 123 patients examined in his 2004 article does not support his conclusion that all patients in Libby with pleural changes are at increased risk of loss of lung function is apparent from the paper itself. The population studied in the paper was predominantly former Grace workers who had far higher asbestos exposures than the great majority of the current Libby population, which is made up mostly of persons exposed to asbestos in the community. Extrapolating the expected lung function decline observed in a population made up of heavily exposed Grace asbestos workers to the much more lightly exposed community cases is no more valid than it would be to extrapolate the lung function decline observed in a cohort of two pack-a-day smokers to a population of 3 cigarette-a-day smokers.

In his paper, the vast majority of the 123 patients in the study are either former Grace workers (86/123) or family members of former Grace workers (22/123). It is well documented that the level of exposure to asbestos in Grace workers who worked at Grace facilities during the 1950 to 1975 time frame mentioned in the study would have been far higher than exposures measured in the Libby community generally. (It is also well documented that asbestos exposures of family members of asbestos workers can be very high as a result of the workers bringing home asbestos dust on their clothes). Indeed, Dr. Whitehouse notes that 45 % of the 123 patients had some evidence of interstitial lung disease, and not just pleural changes. The fact that, on average, there were small, non-clinically significant, but nonetheless observable declines in FVC, TLC and DLCO in the 123 patients studied does not allow one to conclude that the entire 1500 patient Libby Cohort, the majority of whom are community exposure cases, will suffer similar lung function declines. To support that assertion, Dr. Whitehouse would need to have a longitudinal study across the entire Libby cohort, not just a cohort of individuals that were predominantly former Grace workers.

(2) The study is composed of 123 patients, and so is not actually comparable to a cohort of Libby residents. His patients would be expected to be more likely to have respiratory symptoms than the larger group of asbestos-exposed persons in Libby, and Dr. Whitehouse does note that many of the subjects used a variety of bronchodilators. Individuals with respiratory symptoms have a more rapid loss of lung function over time. An analysis from the Six Cities Study found that in an adult population sample of 3,948 subjects (1,757 men; 2,191 women) followed for 12 yr, reporting of any respiratory symptoms was associated with both a reduction in initial lung function and more rapid decline in height-adjusted FEV1. After adjustment for height, age, and cigarette smoking, men with cough or phlegm showed accelerated loss in FEV1.

(3) Height was adjusted to match across study dates if different heights were recorded on the date of first and last test. (The paper does not state whether the taller or shorter height was chosen.) If an individual had truly lost height due to vertebral compression this adjustment would give him a greater loss over time, since the predicted values assigned by this correction would be higher than the true predicted value.

(4) Accelerated lung function decline is seen in current smokers. Whitehouse reports that 7% of the study population was current smokers, but since he presents all his results as averages for the entire group the accelerated decline in current smokers could impact the overall results. Xu et al report that the accelerated rate of loss of FEV1 among smokers depended linearly on the number of cigarettes smoked per day during the interval between examinations with an estimated increase in rate of loss associated with smoking of 12.6 ml/yr per pack/day for men; for a 2 pack/day smoker this would be a loss of lung function of 75 ml over a 3 year period beyond what would be expected from aging.

(5) Dr. Whitehouse uses cross-sectional data [4] to predict longitudinal change. He used the predicted values from Knudson for FVC, which are from a cross-sectional sample. Ware and Dockery report that in the Six Cities Study the individual rates of loss among health non-smokers increased more rapidly with age than what was predicted from a cross-sectional model. For example, for a male of height 1.75 m, the cross-sectional model predicted an increase in the annual rate of loss of FEV1 from 23.7 ml/yr at age 25 to 39.0 ml/yr at age 75, while the longitudinal model gave rates of loss increasing from 12.9 ml/yr at age 25 to 58.2 ml/yr at age 75. This study suggests that the actual drop in lung function in a 75 year old would be 50% higher than anticipated using a cross sectional population to estimate change.

(6) The predicted values used in Dr. Whitehouse's analysis actually have few data points in the age range of his population, making the "expected" loss of lung function with age subject to a wide confidence interval. He reports an average age of 66 at the first test and 69 at second test.

[4] Cross-sectional data is data taken at one point in time. In this case it means that the 40-year-olds and 60-year-olds are different people both studied in the same year, rather than studying the same individual at age 40 and then 20 years later at age 60.

(7) Increase in BMI can cause a decrease in lung function, as Dr. Whitehouse discusses in his paper. He reports that the average increase in BMI was less than 1 kg/m2. Research shows that an increase in BMI of 1 kg/m2 would be, on average, associated with a 16 ml decline per year, or about a 45 ml decline over the course of this study. In combination with the other factors noted, this average increase in BMI could contribute to the loss of lung function measured.

(8) The paper purports to measure loss of lung function attributable to pleural disease, but 45% of the study population had interstitial changes on HRCT or chest x-ray. There actually were only 67 patients with pleural disease and no interstitial disease.

(9) The most important limitation to Dr. Whitehouse's study may be the definition of change over time. Because spirometry is used in occupational medical monitoring programs and in epidemiological studies of lung function, there is a good deal of research available on variability in FVC and FEV1, and how that variability affect interpretation of change over time.. The American College of Occupational and Environmental Medicine (ACOEM) developed recommendations on the use on spirometry to measure change over time:

"Although "using the subject as own his/her own control" may detect pulmonary function declines that are missed by comparisons with predicted values, practitioners who analyze longitudinal spirometry data are often unaware of the pitfalls that can invalidate their conclusions. Since both technical and biological factors affect spirometry results at each test session, practitioners should attempt to hold these factors constant if longitudinal analysis is anticipated. Failure to control these factors produces extraneous variability which may be interpreted as an excessive loss or gain of lung function. Therefore, users of spirometry data should appreciate the effects of technical and biological factors on measurements and be prepared to evaluate test quality and reject inadequate tests before evaluating change over time."

The ACOEM guidelines describe technical and biological factors that affect test to test variability. Dr. Whitehouse has testified that his technicians followed American Thoracic Society (ATS) guidelines for all testing. I did not review any supporting documentation on the testing so cannot validate or dispute his statements on technician training, test procedures, and equipment calibration. But even if all tests met the ATS criteria for reproducibility and calibration of equipment met all specifications, there are other factors listed in the ACOEM guidelines that appear particularly important here:

(a) The recommendation to minimize unnecessary equipment changes **"**Unnecessary equipment changes should be avoided if longitudinal analysis of results is anticipated, though excessively variable spirometers should be replaced by instruments with greater precision. The ATS recommends that spirometers should be accurate to within +/-3% of the volume introduced into a spirometer, so a spirometer meets minimum criteria for accuracy if it records between 2.91-3.09 liters when a 3.00 liter volume is introduced. But since variability exists both within and between spirometers, a 3-liter subject could record 3.09 liters on one spirometer and 2.91 liters on a different spirometer, even though both spirometers met minimum accuracy requirements. Some variation between spirometers may be due to their different mechanisms for determining volume or their use of variable

disposable sensors. Some flow-type spirometers measure slightly different volumes when air passes through the sensor at different speeds, while volume-type spirometers are less affected by the speed of air entering the spirometer. Some spirometer sensors may also be subject to changes in calibration over time."

Dr. Whitehouse reports in the paper that studies prior to 1998 were conducted on a Sensormedics 6200, and subsequent ones on a Medigraphics 1085, and that the same technician performed all testing. Review of medical records from the patients specifically noted by Dr. Whitehouse to have rapid progression or pleural deaths shows that patients were tested in 4 different facilities; the Physician's Clinic of Spokane, the Spokane Pulmonary Clinic, the Spokane office of Drs. Klock and Whitehouse, and the Center for Asbestos Related Disease in Libby.

(b) ***Minimize biological variability*** "As airway caliber changes, spirometry measurements demonstrate diurnal (within a day) and seasonal (within a year) variability, so that time of day and year should be standardized when collecting serial measurements for long-term longitudinal analysis. Though diurnal variability, in particular, gives important information when short-term changes are evaluated, *e.g.*, due to asthma, these factors should be controlled when long-term change in function is the outcome of interest. Many medical surveillance programs conduct examinations on the employee's birthday, so that seasonal variability is controlled. Other factors may also affect test results and should be queried before conducting a spirometry test. NIOSH recommends that testing be postponed for three weeks if the subject has had a recent severe respiratory infection. The test should be postponed for one hour if the subject has had a large meal, smoked a cigarette, or used a bronchodilator within the last hour. The one hour postponement can sometimes be achieved by performing the spirometry test later in a physical examination. If it is not feasible to postpone a test, these factors should at least be documented on the report of test results."

The ACOEM statement cautions: "Because measurement variability strongly affects estimates of change in lung function over time, the expected rate of change is not as well defined as the cross-sectional "predicted" value."

"ACOEM recommends simple methods for comparing an employee's periodic spirometry results with a ***Longitudinal Lower Limit of Normal (LNL)*** specific for that employee. Starting with an individual's baseline lung function level, the LNL describes the lowest results that might be expected for his/her lung function during follow-up, due to normal aging and measurement variability. Test results falling below the LNL may indicate significant deterioration of pulmonary function. However, to make such evaluations possible, spirometry data must be collected carefully, following standardized protocols. *The rate of false positives will be high if test variability is not minimized through QA protocols, standardized testing procedures, and the continuity of well-maintained equipment*."

"A "significant" decline should exceed both: 1) year-to-year measurement variability, currently estimated at 15%; and 2) the expected age-related decline, which can be calculated as the difference between the baseline and follow-up predicted values. These

factors are used below to determine the LNL for follow-up test results. An employee is expected to remain above the LNL as he/she ages."

The ATS also notes that technical and biological variability from test to test can result in up to a 15% difference in FVC.

ACOEM states "Once a worker is identified as having impaired lung function, ATS recommends a less conservative definition for evaluating progression of disease, since both the measured volumes and the percents of predicted are smaller than for the healthy individuals discussed above. In the statement on "Idiopathic Pulmonary Fibrosis: Diagnosis and Treatment," ATS and the European Respiratory Society (ERS) recommend interpreting *a loss of 10% or more of the measured baseline VC (or at least 0.20 L)* as a "failure to respond to therapy," *i.e*., a significant decline, if the change is accompanied by parallel changes in single-breath diffusing capacity or oxygen saturation 6 months after the baseline test. In addition, *an increase from the measured baseline VC of 10% or more (or at least 0.20 L)* is interpreted as a significant improvement if the change is accompanied by parallel changes in single-breath diffusing capacity or oxygen saturation and is maintained for two consecutive visits within a 3-6 month period. *Changes smaller than +/- 10 % of measured baseline VC (or < 0.20 L)* maintained for two consecutive visits within a 3-6 month period indicate stable pulmonary function."

(10) Variability in DLCO (diffusion capacity for carbon monoxide)

The standard for reproducibility of DLCO is that at least 2 acceptable tests are within ± 10% or 3 mL CO(STPD)/min/mm Hg of the average DLCO. This means that the acceptable test to test variation is least 10%. The ATS statement on DLCO cites a 9% variation in normal individuals over a one year period.

DLCO depends upon a number of physiologic factors. Besides varying with age, sex, and height DLCO also changes with hemoglobin (Hb), lung volume, COHb, inspired pressure of oxygen (altitude), exercise and body position. The American Thoracic Society recommends that specific adjustment for hemoglobin, COHb, and inspired pressure of oxygen (altitude), should always be made to ensure appropriate interpretation. These specific equations are included in the ATS document on diffusion capacity. For example, the pressure of inspired oxygen in arterial blood (PIO2) at sea level is 149 mmHg. At 2000 ft (the altitude in Libby Montana) PIO2 define drops to approximately 139 mmHg. DLCO changes by approximately 0.31% per mmHg decrease in PIO2, so will change approximately 3% between sea level and 2000 feet. Without adjustment for this change in altitude the predicted value will be inaccurate. A Hb define of 13 would require an adjustment in the predicted DLCO to 95% of the value predicted without adjustment, which assumes a Hb of 14.6. I reviewed a number of PFTs from the patients treated by Dr. Whitehouse and saw no time where values were adjusted for hemoglobin or PIO2. A few percentage change in predicted value may not be clinically significant, but since Dr. Whitehouse concludes that a change of 2-3% per year in DLCO indicates rapid progression this small change in predicted values could affect these conclusions.

> It is also recognized that large inter-laboratory differences in measured DLCO and in percent-of-predicted DLCO exist; these are attributed to variations in testing techniques and computational algorithms and errors in gas analysis. The choice of equipment may also influence the measured DLCO. The ATS states that a single value cannot be recommended for all labs (2005), and that ideally labs should choose predicted values that best match results on healthy individuals in each lab. The patients in Dr. Whitehouse's study had pulmonary testing in a number of laboratories over time: Physician's Clinic of Spokane, the Spokane Pulmonary Clinic, the Spokane office of Drs. Klock and Whitehouse, and CARD. Even if the test results were all compared to the same set of predicted values the inter-laboratory differences in measured values would certainly affect measurement of change over time.
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> Because there is so much inter-laboratory and test-to-test variation in DLCO, and because the test results presented in the Whitehouse 2004 paper were not adjusted for hemoglobin or altitude, it is my opinion that the change reported over time in the range of 6% over three years is not likely to be clinically or statistically significant.

In his analysis of progression of lung function over time, Dr. Whitehouse chose to compare the loss of lung function seen among his patients to the loss that would be expected based on predicted values, rather than using a statistical model. The standards and recommendations for primary function testing presented here from ATS and ACOEM allow us to conclude that a change of less than 15% in spirometry values, or change of less than 9% in DLCO could be due to test to test variation. Dr. Whitehouse describes an average change of 6.4% in FVC, 6.8% in TLC, and 8.7% in DLCO over a three-year period. Given the test to test variation in these parameters this change could be due solely to chance.

In addition there are range of other factors which suggests his patients would have more rapid loss of lung function than an average healthy population, since he included some patients who were current and ex-smokers, patients who had respiratory symptoms, and patients being treated with bronchodilators presumably for some obstructive lung disease. As described above, all these groups would be expected to have lung function loss that exceeded what one would see due to aging alone.

There is very little information that allows us to know what rate of pulmonary function loss to expect in individuals with parenchymal asbestosis. Since almost half of Dr. Whitehouse's patient population had parenchymal asbestosis, one would not be surprised to see lung function loss in excess of what is due to aging in a healthy population.

Review of selected patient files in progression study:

Dr. Whitehouse identified 18 individuals as having rapid progression of pulmonary function loss, and I have reviewed 13 of those cases in detail. (I could not find any records for two of the individuals listed (CC, LH), nor are these individuals listed in the master crossover sheet. Three others were not part of the progression study (RM, VH, DA) so were not included in my review

relative to progression.) Review of these cases shows that my concerns outlined above apply in this population studied by Dr. Whitehouse.

Two of the individuals had diffuse pleural thickening, which can be associated with significant pulmonary function impairment. Accelerated decline in someone with this disease would not be unexpected.

Five individuals had significant obstructive lung disease, and as noted above obstructive lung disease is associated with the more rapid decline in pulmonary function.

For six of these 13 cases I had significant concerns about the validity of the testing:

(1) two individuals were measured to be taller as the years went by, which then was reflected in a decreased percent predicted for diffusion capacity; the actual value was unchanged.

(2) for two others the predicted values changed significantly

(3) four individuals had diffusion capacities that were not valid but it appears the physician conclusions in the medical records were based on this invalid testing.

D. Dr. Whitehouse's opinion that Libby amphibole is more toxic than other forms of asbestos.

On page 44 Dr. Whitehouse details his opinion that amphibole asbestos in general, and Libby asbestos in particular, is more carcinogenic and fibrogenic than chrysotile asbestos. He uses this line of argument to support his conclusions that the rate of disease seen among his patients in the CARD clinic is higher than what has been seen in other asbestos exposed cohorts, and to support his opinion that he sees rapid progression of asbestos related disease among his patients.

On page 44 he implies that the official statement from the ATS concurs with this opinion (see item 53). The ATS document does include the statement that chrysotile fibers are cleared more efficiently than amphibole asbestos fibers, but the document does not conclude that the amphiboles have greater toxicity than chrysotile. Dr. Whitehouse's use of the quotation from the ATS document is misleading.

National and international public health agencies agree that all asbestos fiber types cause lung cancer, mesothelioma, other asbestos-related cancers, and nonmalignant respiratory disease. Although there may be a difference in cancer potency on a fiber per fiber basis among the different types of asbestos, this difference is often not relevant to question of whether a given exposure contributes to the injury suffered by an individual with asbestos-related disease. The U.S. Public Health Service Toxicological Profile for Asbestos (2001) states: "There is general agreement among scientists and health agencies . . . [e]xposure to any asbestos type (i.e., serpentine [chrysotile] or amphibole) can increase the likelihood of lung cancer, mesothelioma, and nonmalignant lung and pleural disorders.". Many other reviews support this conclusion, such as those from the American Conference of Governmental Industrial Hygienists [(2)], the American Thoracic Society [(3)], the Environmental Protection Agency [(4)], the International Agency for Research on Cancer [(5)], the National Toxicology Program [(6)], the Occupational Safety and Health Administration [(7)], the Consumer Products Safety Commission ("CPSC") [(8)], and the World Health Organization [(9-11)], and the World Trade Organization [(12)]. Even if there is a differential risk of malignant or nonmalignant asbestos-related disease on a fiber per fiber basis, all fiber types cause these diseases.

Dr. Whitehouse stated that chrysotile fibers are cleared more efficiently than amphibole asbestos fibers from the lung. Although it does appear that chrysotile fibers are rapidly cleared from the human lung, and not commonly found in large quantity at autopsy, the importance of persistence in the lung as a specific risk for cancer is highly speculative. Chrysotile fibers are very potent carcinogens in animal models. High lung cancer rates are reported in the chrysotile textile industry, and recent papers by Yano [5]and Pan [6] show excess lung cancer among workers exposed to amphibole free chrysotile asbestos.

Dr. Whitehouse references Berman and Crump (2003) to support his opinion that Libby amphibole is more dangerous than other asbestos exposures occurring to workers using WR Grace products. The model developed by Berman and Crump proposed to assessing risk of mesothelioma and lung cancer from asbestos, incorporating fiber type and fiber dimensions. The EPA appointed peer review committee agreed that an updated risk assessment would be valuable but did not support the one presented; that risk assessment was never adopted by the US Environmental Protection Agency. In 2008 EPA convened its Scientific Advisory Board to review a new risk assessment model, again developed by Drs. Brattin and Crump, to assign fiber type and dimension-specific risks. After reviewing the 2008 proposal, the SAB Asbestos Committee concluded "there is sufficient evidence to support the need for the Agency's effort in developing risk assessment method(s) to account for potential differences in risk on the basis of mineral type and size characteristics of asbestos."[7] However, the Committee also "generally agreed that the scientific basis as laid out in the technical document in support of the proposed method is weak and inadequate. A primary concern is the lack of available data to estimate the TEM specific levels of exposure for the epidemiological studies utilized in this analysis." At the current time OSHA, NIOSH and EPA have not announced any plans to undertake another asbestos risk assessment, and it is still the official position of the US government that one fiber type is not clearly more carcinogenic than others. [8]

Dr. Whitehouse also references a paper by Hodgson and Darnton (2000) which focuses on risk assessment for the risk of cancer from asbestos. This paper supports the view that amosite is more potent than chrysotile, on a fiber per fiber basis, for the development of mesothelioma. There is no consensus on the relative potencies of fiber types for non-malignant disease and lung cancer [9]. However for the purposes of this trust distribution process the question of fiber potency for mesothelioma is not relevant to asbestosis and particularly to the risk of progressive non-

[5]Yano E, Wang ZM, Wang XR, Wang MZ, Lan YJ. Cancer mortality among workers exposed to amphibole-free chrysotile asbestos. Am J Epidemiol. 2001 Sep 15;154(6):538-43.
[6] Pan XL, Day HW, Wang W, Beckett LA, Schenker MB. Residential proximity to naturally occurring asbestos and mesothelioma risk in California Am J Respir Crit Care Med. 2005 Oct 15;172(8):1019-25.
[7] Letter from Agnes Kane, Chair SAB Asbestos Committee to Stephen Johnson, Administrator U.S. EPA. 11/14/2008
[8] Environmental Protection Agency. Airborne Asbestos Health Assessment Update. EPA/600/8-84/003F, 1-197. 1986. Springfield VA, NTIS
[9] Stayner, LT. Canada, chrysotile and cancer: Health Canada's asbestos international expert panel report. J Occup Environ Med. 2008 Dec;50(12):1327-8.

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malignant disease. Risk assessments developed to determine the risks of mesothelioma and lung cancer are not relevant to the discussion of progressive nonmalignant pulmonary disease.

There is very little information about the rate of asbestosis in populations exposed predominately to chrysotile. One cohort is the chrysotile textile plant in South Carolina study by Dement and colleagues; this plant was reported to have a high rate of asbestosis. Stayner recently published a detailed analysis of exposure response relationships in a this plant using new TEM-based exposure estimates. Stayner stated that evidence from toxicological studies indicates that the risk of respiratory diseases varies with asbestos fibre length and width but there is no epidemiological evidence concerning this question. The TEM-based cumulative exposure estimates were found to provide stronger predictions of asbestosis than prior PCM-based estimates. Cumulative exposures based on individual fibre size-specific categories were all found to be highly statistically significant predictors of asbestosis. Asbestosis was most strongly associated with exposure to thin fibres (<0.25 microm). Current PCM-based methods may underestimate asbestos exposures to the thinnest fibres, which were the strongest predictor of asbestosis mortality in this study.

Dr. Whitehouse compares the rate of disease reported in the medical literature to draw conclusions about the rate of progression of asbestosis in cohorts exposed to chrysotile versus amphibole. His analysis simplifies the studies and he does not include all the relevant studies in his discussion. The table below includes some additional information on the studies cited by Dr. Whitehouse, and also includes studies not cited by Dr. Whitehouse that have also looked at progression in asbestos exposed populations.

One can see in the table that the median latency to first x-ray varies considerably. Given that the minimal latency for asbestosis is estimated as 20 years in the United States (American Thoracic Society 2004), more “progression” from a normal to an abnormal radiograph would be expected in studies with a short latency at the time of the first radiograph; if a cohort did not have sufficient latency to have developed asbestosis by time of first x-ray clearly one would expect more change over time. The study by Sluis-Kremer, which had only 5.5 years from first exposure to first x-ray, would be expected to have a higher rate of radiographic change between first and second x-ray then a study such as the one reported by Jones, which had over 20 years of latency at the time of the first x-ray.

Dr. Whitehouse does not discuss the study by Viallet (1983) which shows that 39% of those with a normal film on first x-ray progress to a film classified as 1/1 or more; this cohort was exposed to chrysotile asbestos. An additional study not included by Dr. Whitehouse is the one reported by Shepard (1997), which looked at cohort of workers exposed to amosite in asbestos manufacturing. In this group 6% progressed from normal to a film classified as > 1/0; this rate of progression is lower among amosite exposed workers than the rate reported among chrysotile miners in the study by Viallet.

Dr. Whitehouse includes the papers by Gregor (1979) and Cookson (1986) in his analysis. Both were studies of individuals who had applied to a Pneumoconiosis Board for compensation of asbestosis and not population-based cohorts; it is not appropriate to use these studies in comparison to population-based cohorts, since a group of patients differs in important ways from

the larger group of exposed workers from which they come. These differences were discussed above.

Looking at these studies altogether, it is my opinion that it is not possible to isolate the effect of fiber type given that the dose of asbestos, latency, years of exposure, years of follow-up, and even the basic structure of the cohort all very greatly between the studies [10].

[10] Sluis-Cremer GK, Hnizdo E. Progression of irregular opacities in asbestos miners. Br J Ind Med. 1989 Dec;46(12):846-52; Ehrlich R, Lilis R, Chan E, Nicholson WJ, Selikoff IJ. Long term radiological effects of short term exposure to amosite asbestos among factory workers.Br J Ind Med. 1992 Apr;49(4):268-75; Jones RN, Diem JE, Hughes JM, Hammad YY, Glindmeyer HW, Weill H. Progression of asbestos effects: a prospective longitudinal study of chest radiographs and lung function. Br J Ind Med. 1989 Feb;46(2):97-105; McMillan GH, Rossiter CE. Development of radiological and clinical evidence of parenchymal fibrosis in men with non-malignant asbestos-related pleural lesions. Br J Ind Med. 1982 Feb;39(1):54-9; Shepherd JR, Hillerdal G, McLarty J. Progression of pleural and parenchymal disease on chest radiographs of workers exposed to amosite asbestos. Occup Environ Med. 1997 Jun;54(6):410-5; Becklake MR, Liddell FD, Manfreda J, McDonald JC. Radiological changes after withdrawal from asbestos exposure. Br J Ind Med. 1979 Feb;36(1):23-8

Study [11]	**Exposure period and location**	**Exposure: fiber type and average exposure metric to first x-ray**	**Median latency 1st x-ray**	**Median latency 2nd x-ray**	**Incidence 1st to 2nd x-ray**	**Predictors of progression (Cases with asbestos-related disease on first x-ray and with normal first x-ray combined.)**
Becklake 1979	Quebec miners, exposed before 1961 mean of 10 yrs	Chrysotile Mean 236 mpcf-y	11	28	Progression from normal radiograph: 6% parenchymal, 17% pleural.	Duration of exposure, cumulative exposure for parenchymal; no predictors for pleural (univariate analysis)
McMillan 1982	UK shipyard, exposures 1940-1966	No measurements available	21.5 yrs	31.5 yrs	13.1% of those with pleural disease only at 1st x-ray developed opacities 1/1 or higher	Not reported
Viallet 1983	Mine and mill in Corsica, exposures 1948-1965	Chrysotile 29.7 dust-weighted years *	13	28	39% of those with 0/0 film on 1st x-ray progressed to >1/1	Age, cumulative exposure, smoking (univariate analysis)
Sluis-Cremer 1989	South African asbestos mines with exposures 1965-1975	Amphibole 38.4 f/yrs, mean of 5.5 yrs worked	5.5	11	Progression from 0/0 radiograph to >1/0: 11.5%. Progression from 0/1 radiograph to >1/0: 63%.	Age, duration of exposure prior to 1st x-ray, years between x-rays, profusion on 1st x-ray, and smoking (multivariate analysis)
Jones 1989	Asbestos cement plants, exposures beginning in 1950s, examinations in 1970 and 1980	Chrysotile with some crocidolite Mean 138 mppcf-y	21.3	31	Progression from 0/0 radiograph to >1/0: 10.1%. Progression from normal radiograph to any pleural disase: 16.9%	Average and cumulative dust exposure for parenchymal and pleural. Those with disease had more progression than those with normal films on 1st x-ray (multivariate analysis).
Ehrlich 1992	Paterson NJ asbestos manufacturing , exposure 1941-1954	Amosite 25 f/yrs	26.5	35	Progression from normal radiograph: 10% parenchymal, 21% pleural.	Cumulative exposure for parenchymal; latency for pleural (multivariate analysis).
Shepard 1997	Tyler TX asbestos manufacturing	Amosite Mean 53 f/yrs	11	21.6	Progression from 0/0 to > 1/0: 5.9% Progression from normal to any pleural disease: 17.2%	Age, duration of exposure, latency, smoking for parenchymal. For pleural change, dose and duration were significant (multivariate analysis)

Dr. Whitehouse's criticism of the diagnostic criteria set forth in the TDP

Dr. Whitehouse states that it is arbitrary to requirement use of the 2000 edition of the ILO Classification of Pneumoconiosis for a finding of diffuse pleural thickening, including the width and extent requirements and the requirement that there be blunting of the costophrenic angle. The ILO classification system, which was described in more detail in my December 31, 2008 report, has consistently been used for both epidemiological purposes and by medical practitioners as a shorthand way to read x-rays both for diagnosis and assessment of severity. Although this classification was not designed for clinical diagnosis it is a standard notation for describing dust diseases on the chest x-ray, and has been very useful in a number of settings. The alternatives are (1) to accept the statement from any doctor that there is asbestos related disease on radiograph, or (2) to require all radiographs to be read by a panel of experts. The first option contains no criteria for training or standardization, and the second option would be cumbersome and expensive. The ILO classification has been shown to correlate with both dust deposition in the lung and the severity of pulmonary function impairment. [12] In my opinion it is medically reasonable to base the TDP around the ILO classification.

The 2000 update of the classification was developed by a panel of experts, who reached agreement on the recommendations. The list of experts is listed in appendix F of the guidelines, and includes experts from around the world. The introduction to the new classification describes the extensive process used for the update. The rationale for including the requirement for blunting of the costophrenic angle is described in the instructions for the 2000 revision (International Labour Office (ILO). *Guidelines for the Use of the ILO International Classification of Radiographs of Pneumoconioses, Revised Edition 2000* (Occupational Safety and Health Series, No. 22). International Labour Office: Geneva, 2002.)

There is strong scientific rationale for requiring blunting of the costophrenic angle in determining which pleural scarring causes significant impairment, and this is the role of the presumptions in the TDP. The criteria are set to easily identify those individuals who clearly have impairment from exposure to asbestos, and to define what level of impairment will be compensated. The study by Lilis [13] included over 1500 individuals with asbestos-related pleural disease, and showed that individuals with diffuse pleural fibrosis, defined as involving the costophrenic angle, had significantly lower FVC than individuals with circumscribed pleural scarring.

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[12] Miller A, Lilis R, Godbold J, Wu X. Relation of spirometric function to radiographic interstitial fibrosis in two large workforces exposed to asbestos: an evaluation of the ILO profusion score. Occup Environ Med. 1996 Dec;53(12):808-12; Miller A, Lilis R, Godbold J, Chan E, Selikoff IJ. Relationship of pulmonary function to radiographic interstitial fibrosis in 2,611 long-term asbestos insulators. An assessment of the International Labour Office profusion score. Am Rev Respir Dis. 1992 Feb;145(2 Pt 1):263-70.

[13] Lilis R, Miller A, Godbold J, Chan E, Selikoff IJ. Pulmonary function and pleural fibrosis: quantitative relationships with an integrative index of pleural abnormalities. Am J Ind Med. 1991;20(2):145-61

There may be individuals who have significant diffuse pleural thickening but do not meet the criteria set by the ILO classification. In that case these individuals can have an individual review which is based on interpretation of a high-resolution CT scan. Dr. Whitehouse states that in his mortality study, of the patients who died of nonmalignant asbestos disease 83% met the 3 mm minimum thickness requirement on chest x-ray, and the same percent met the requirement for an extent greater than 25% of the chest wall (there is likely to be substantial overlap between the groups that did not meet each of these criteria). As noted above it is my opinion that Dr. Whitehouse attributes more deaths to asbestos related disease than should be so attributed; it is therefore likely that substantially fewer than 17% of Libby claimants with diffuse pleural thickening would require individual review.

Dr. Whitehouse stated that diffusion capacity should be included in the TDP as a measure of severity. As described in my December 31, 2008 report, it is my opinion that DLCO is not considered either a reliable or specific enough test to use as a presumption for compensation in the TDP. As described in my December report and in this report, there is substantial variability in the test within and between testing days, and there is no agreed-upon set of predicted values. Dr. Whitehouse is correct that DLCO is a routine part of the clinical evaluation of asbestosis and other interstitial lung diseases, and DLCO is recommended by the American Thoracic Society as part of the evaluation of asbestosis. However, DLCO is also decreased in emphysema, and therefore a reduction in DLCO is less specific for interstitial lung disease than is a reduction in lung volumes. A reduced DLCO with a normal TLC and normal FVC could be due to emphysema or some other interstitial lung disease and not asbestosis.

Dr. Whitehouse stated that in his opinion it was inappropriate to use the FEV1/FVC ratio as part of the criteria, since to do so would exclude individuals with obstructive lung disease. As described in my December 31, 2008 report, it is my opinion that an individual evaluation would be needed to determine if significant asbestos related impairment was present in someone who had significant obstructive lung disease. The criteria set forth in the TDP are presumptions. An individual who does not meet these criteria can apply for an individual evaluation. When the FVC is used to measure the presence and extent of restrictive impairment, the TDP requires that the FEV1/FVC ratio must be greater than 65%. Setting the lower limit of the FEV1/FVC ratio at 65% will exclude claimants who have an obstructive defect from asthma, asbestosis or smoking. If a claimant has several co-existing medical conditions such as asbestosis and COPD from smoking, it is my opinion that an individual evaluation would be needed to determine if the asbestosis was a substantial contributing factor to the impairment.

Dr. Whitehouse stated that an FEV1/FVC ratio of greater than 65% would exclude those with an obstructive component to their asbestos pleural disease. This is not true. Obstructive disease is defined as an FEV1/FVC ratio of less than 70%. Setting the ratio at 65% allows individuals with obstructive disease to receive compensation under the presumptions, but limited to those with a relatively mild form of obstruction, or a mixed obstructive restrictive disease. Dr. Whitehouse states that the ATS statement on diagnosis of nonmalignant disease from asbestos does not include a requirement of an FEV1 FVC ratio over 65%. This is true but also is misleading,

because the ATS statement does not require **any** pulmonary function testing for a diagnosis of asbestos related disease.